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09/230,048	03/12/99	FLECKENSTEIN B	058315/0129

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1633	9

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/230,048	Applicant(s) Fleckenstein et al.
	Examiner Janet M. Kerr	Group Art Unit 1633

☒ Responsive to communication(s) filed on *Jul 17, 2000*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-20 and 28-35* is/are pending in the application.

Of the above, claim(s) *13-15, 17, and 29-33* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-12, 16, 18-20, 28, 34, and 35* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

X Notice of Sequence Compliance

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

The preliminary amendments, filed 3/12/99 and 7/17/00, have been entered.

Claims 21-27 have been canceled.

Claims 28-35 have been added.

Claims 1-20 and 28-35 are pending.

Election/Restriction

Applicant's election of Group I, claims 1-12, 16, 18-20, 28, 34, and 35 in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).Claims 13-15, 17, 29-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 6.

Claims 1-12, 16, 18-20, 28, 34, and 35 are being examined on the merits.

Specification

The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

The following order or arrangement is preferred in framing the specification and, except for the reference to "Microfiche Appendix" and the drawings, each of the lettered items should appear in upper case, without underlining or bold type, as section headings. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) Title of the Invention.
(b) Cross-References to Related Applications.
(c) Statement Regarding Federally Sponsored Research or Development.
(d) Reference to a "Microfiche Appendix" (see 37 CFR 1.96).
(e) Background of the Invention.

1. Field of the Invention.
2. Description of the Related Art including information disclosed under 37 CFR 1.97 and 1.98.

(f) Brief Summary of the Invention.
(g) Brief Description of the Several Views of the Drawing(s).
(h) Detailed Description of the Invention.
(I) Claim or Claims (commencing on a separate sheet).
(j) Abstract of the Disclosure (commencing on a separate sheet).
(k) Drawings.
(l) Sequence Listing (see 37 CFR 1.821-1.825).

The disclosure is also objected to because of the following informalities: on page 3, under part d), it is not clear what "b1" represents; on page 4, last line of part I), it is not clear what applicants intended by the phrase "shall be comprised"; on page 5, part p) the phrase "v-IL-6 or the polypeptide" is confusing, i.e., what is the distinction between v-IL-6 and the polypeptide? And in part r, the term "auxilliary" should be changed to "auxiliary"; on page 6, part v), the term "hemopoetic" should be changed to "hemopoietic" if applicants intended hemopoietic, and the name "california" should be capitalized; and on page 7, last line in the description of Fig. 1, the reference of M. Dayhoff is incomplete; on page 7, under "Bibliography", references 3, 4, and 7 are incomplete.

Appropriate correction is required.

Claim Objections

Claim 8 is objected to because of the following informalities: the term "competively" should be changed to "competitively". Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are directed to viral interleukin-6 (claim 1) and a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 (claims 2-3). As written, the claims read on proteins/polypeptides which are found in nature (the polypeptides *can be* obtained but are not necessarily obtained by recombinant expression) and thus, are unpatentable to the applicant. It is suggested that applicants amend the claims to indicate that the polypeptides are "isolated and/or purified", using language which has antecedent basis in the specification and which clearly indicates that the claimed invention is not a product of nature.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-7, 8, 12, 18, 19, 34, and 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants are referred to the revised interim guidelines on written description published December 21, 1999 in the Federal Register at Volume 64, Number 244, pp. 71427-71440 (also available at www.uspto.gov).

Claims 18 and 19 are directed to pharmaceutical compositions comprising as an active ingredient, v-IL-6 (claim 18) or nucleic acid sequence encoding v-IL-6 (claim 19) and a pharmaceutically acceptable carrier. While the specification discloses a medicament wherein the active ingredient is combined with suitable excipients and/or other auxiliary compounds (see page

5, section r of the specification), the phrases "pharmaceutical compositions" and a "pharmaceutically acceptable carrier", added by applicants' amendment, are new matter as the phrases are neither supported by the teachings in the specification nor the claims as originally filed. This is a new matter rejection.

Claims 34 and 35 are directed to a method of culturing cells comprising adding to a cell culture a cell growth-stimulating amount of v-IL-6 (claim 34) wherein the cells are selected from b-lymphocytes, hybridomas, hemopoetic (sic) or endothelial cells (claim 35). The phrase "a cell growth-stimulating amount of v-IL-6", added by applicants' amendment, is new matter as the phrase is neither supported by the teachings in the specification nor the claims as originally filed. The specification, on page 6, part v) discloses a process of growing cells in a culture medium comprising v-IL-6, or v-IL-6 mutants, variants, fragments, or mixtures thereof. There is no support in the specification of "a cell growth-stimulating amount of v-IL-6". Thus, based on the disclosure as filed, the specification only contemplates a method of growing cells in medium comprising v-IL-6 or fragments, mutants or variants of v-IL-6. It is not readily apparent that this limited information would reasonably convey to one skilled in the art that applicants had adequately described appropriate amounts of v-IL-6 to stimulate growth of cells. This is a new matter rejection.

Claims 4-7 are directed to fragments of v-IL-6 which have the capability of binding to an IL-6 receptor. The specification teaches that the area involved in binding of human IL-6 to its receptor has been mapped to the middle of the protein by two groups, one of which demonstrates that amino acids 105 to 123 of the human IL-6 are involved in receptor binding. The specification indicates that this region is highly conserved in v-IL-6, and the degree of conservation of this region of the v-IL-6 is almost identical to the degree of conservation observed in the receptor binding area of human IL-6 relative to murine IL-6. The specification further indicates that as both human IL-6 and murine IL-6 are able to bind to the receptor of the other species, it is likely that v-IL-6 is also able to bind to the human and the murine IL-6 receptor. However, the

specification does not provide any objective evidence that either the full length v-IL-6 or the "IL-6 receptor binding region fragment" is capable of binding to the human or murine IL-6 receptor. In this regard, it should be noted that post-filing art indicates that v-IL-6 binds to gp130, not the IL-6 receptor (see, e.g., Molden *et al.*, J. Biol. Chem., 272:19625-19631, 1997, Wan *et al.*, J. Virology, 73:8268-8278, 1999, Mullberg *et al.*, J. Immunology, 164:4672-4677, 2000, and Hoischen *et al.*, Eur. J. Biochem., 267:3604-3612, 2000). The limited information provided in the specification is not deemed sufficient to reasonably convey to one skilled in the art that applicants were in possession of fragments of v-IL-6 which are capable of binding the IL-6 receptor, at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed fragments.

Claim 7 is directed to mutants and variants of v-IL-6 wherein the mutants and variants are obtained by conventional amino acid substitutions or deletions, with the proviso that these mutants and variants are functionally equivalent to v-IL-6. The specification states that the invention relates to mutants and variants of v-IL-6 or of the polypeptide which can be obtained by recombinant expression of the DNA of HHV-8, and which comprises the amino acid sequence displayed in figure 2, which mutants and variants are obtained by conventional amino acid substitutions or deletions, which the proviso that these mutants and variants are functionally equivalent to v-IL-6. The specification does not disclose, however, a definition of "conventional", nor does the specification provide any sequence data or any guidance as to which specific amino acids can be substituted, which amino acids to use in the substitution, and which amino acids can be deleted such that the mutant or variant of v-IL-6 maintains its functionality. Moreover, as the specification does not provide any object evidence of protein function of v-IL-6, the skilled artisan could not envision mutants or variants of v-IL-6 which can be considered functionally equivalent to v-IL-6. The limited information provided in the specification is not deemed sufficient to reasonably convey to one skilled in the art that applicants were in possession of mutants and variants of v-IL-6 which are functionally equivalent to v-IL-6, at the time the

application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed mutants and variants.

Claim 8 is directed to a fragment of v-IL-6 which competitively inhibits the biological activity of IL-6 in a suitable assay system. While the specification discloses fragments of v-IL-6 which are able to competitively inhibit the biological activity of IL-6 in a suitable assay system (see page 4, section h), the specification does not provide any amino acid sequences of such fragments which inhibit the biological activity of IL-6, what biological activity of IL-6 is inhibited, or which assay is suitable for detecting competitive inhibition. The limited information provided in the specification is not deemed sufficient to reasonably convey to one skilled in the art that applicants were in possession of fragments of v-IL-6 which are capable of competitively inhibiting the biological activity of IL-6 in a suitable assay system, at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed fragments.

Claim 12 is directed to an isolated nucleic acid molecule which hybridizes under stringent conditions to the nucleotide sequence of figure 2.

With regard to nucleic acid molecules obtained by hybridization to the nucleotide sequence of figure 2, the specification fails to provide adequate guidance as to which hybridization conditions are required such that all of the polynucleotides embraced by the claims hybridize to the nucleotide sequence of figure 2 and encode a functionally active v-IL-6. Nucleic acid hybridization assays are extremely sensitive to the conditions in which they are performed. The buffer composition, pH, temperature, length of time, salt concentrations, quality and source of template nucleic acid, are all variables which determine the reproducibility of a given hybridization experiment. For example, Carrico (US Patent No. 5,200,313) discloses factors which affect hybridization reactions including:

1. The purity of the nucleic acid preparation.

2. Base compositions of the probe - G-C base pairs will exhibit greater thermal stability than A-T or A-U base pairs. Thus, hybridizations involving higher G-C content will be stable at higher temperatures.

3. Length of homologous base sequences- Any short sequence of bases (e.g., less than 6 bases), has a high degree of probability of being present in many nucleic acids. Thus, little or no specificity can be attained in hybridizations involving such short sequences. From a practical standpoint, a homologous probe sequence will often be between 300 and 1000 nucleotides.

4. Ionic strength- The rate of reannealing increases as the ionic strength of the incubation solution increases. Thermal stability of hybrids also increases.

5. Incubation temperature- Optimal reannealing occurs at a temperature about 25 - 30°C below the melting temperature for a given duplex. Incubation at temperatures significantly below the optimum allows less related base sequences to hybridize.

6. Nucleic acid concentration and incubation time- Normally, to drive the reaction towards hybridization, one of the hybridizable sample nucleic acid or probe nucleic acid will be present in excess, usually 100 fold excess or greater.

7. Denaturing reagents- The presence of hydrogen bond-disrupting agents, such as formaldehyde and urea, increases the stringency of hybridization.

8. Incubation- The longer the incubation time, the more complete will be the hybridization.

9. Volume exclusion agents- The presence of these agents, as exemplified by dextran and dextran sulfate, are thought to increase the effective concentrations of the hybridizing elements thereby increasing the rate of resulting hybridizations.

10. Further, subjecting the resultant hybridization product to repeated washes or rinses in heated solutions will remove non-hybridized probe. The use of solutions of decreasing ionic strength, and increasing temperature, e.g., 0.1 X SSC

for 30 minutes at 65°C, will, with increasing effectiveness, remove non-fully complementary hybridization products.

Given the numerous variables which impact on the capability of a polynucleotide to hybridize to any other polynucleotide, and given the lack of guidance in the specification as to which hybridization conditions are required such that hybridization can occur and in view of the lack of objective evidence of any "functional activity" of viral-IL-6, the skilled artisan could not envision the structural features of the nucleic acid sequence which hybridizes to the polynucleotide of figure 2 and which has viral-IL-6 functional activity. The limited information provided in the specification is not deemed sufficient to reasonably convey to one skilled in the art that applicants were in possession of nucleic acid sequences obtained by hybridization to a polynucleotide encoding v-IL-6 and which encode functional v-IL-6, at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed nucleic acid sequences.

Claims 4-8, 12, 18-20, 28, 34, and 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 4-6 are directed to a fragment of v-IL-6 which comprises a specific amino acid sequence, and which is capable of binding to an interleukin-6 receptor. The specification, however, does not provide any objective evidence that this amino acid sequence binds to an interleukin-6 receptor. Moreover, as stated in the above written description rejection, Molden *et al.*, Wan *et al.*, Mullberg *et al.*, and Hoischen *et al.*, teach that the v-IL-6 of human herpesvirus 8 does not bind to the IL-6 receptor. Therefore, based on the limited description of binding of this amino acid sequence to an IL-6 receptor

in the specification in the specification, and in view of the teachings in the state of the art that v-IL-6 does not bind to an IL-6 receptor, one of skill in the art would not know how to make or use this fragment such that the fragment binds to an IL-6 receptor.

Claim 7 is directed to mutants and variants of v-IL-6 which are functionally equivalent to v-IL-6. The claim is not enabled as the specification does not disclose any functional characteristics of v-IL-6. The specification indicates that the functional activity of v-IL-6 is thought to be the same as cellular IL-6 in view of the high degree of homology between v-IL-6 and human or mouse IL-6. Moreover, the specification indicates that based on the degree of homology of the human and mouse IL-6 fragments which bind to the IL-6 receptor, and the degree of homology of the v-IL-6 fragment with the human and mouse IL-6 fragments, one would expect that v-IL-6 also binds to the IL-6 receptor via this homologous fragment. The presumption is that binding of v-IL-6 to the receptor will elicit the same functional activity as that observed with the cellular homologues. However, as indicated in the above written description rejection, the teachings of the state of the art indicates that v-IL-6 does not bind to an IL-6 receptor. Given that the initial premise is incorrect, i.e., that v-IL-6 binds to the receptor, one of skill in the art would not have known, at the time of filing, the biological function of v-IL-6. Therefore, one of skill in the art would not know how to make or use mutants and variants of v-IL-6 which are functionally equivalent to v-IL-6 as the function of v-IL-6 has not been disclosed in the instant application.

Claim 8 is directed to a fragment of v-IL-6 which is able to competitively inhibit the biological activity of IL-6 in a suitable assay system. The claim is not enabled as the specification does not disclose any biological activity associated with IL-6, any particular biological activity which can be competitively inhibited by a fragment of v-IL-6, any particular fragment of v-IL-6 which competitively inhibits the biological activity of IL-6, or any suitable assays by which competitive inhibition can be ascertained. Thus, one of

skill in the art would not know which biological activities would be inhibited in an undisclosed assay system.

Claim 12 is directed to an isolated nucleic acid sequence which is hybridizable, under stringent conditions, to an isolated nucleic acid molecule encoding v-IL-6. The claim is not enabled as the specification does not define conditions which are deemed stringent, nor does the specification disclose nucleic acid sequences, other than that encoding HHV8 v-IL-6. Given the numerous variables which impact on the capability of a polynucleotide to hybridize to any other polynucleotide, as discussed under the written description rejection above, and given the lack of guidance in the specification as to which hybridization conditions are required such that hybridization can occur, one of skill in the art would not have had a high expectation of successfully obtaining the claimed polynucleotides without undue experimentation. Moreover, once obtained, the specification does not provide guidance as to how to use these particular polynucleotides.

Claims 18 and 19 are directed to pharmaceutical compositions comprising the v-IL-6 polypeptide (claim 18) or the nucleic acid sequence encoding HHV8 v-IL-6 (claim 19). The claims are not enabled for the pharmaceutical compositions as the specification does not provide guidance as to how to use the compositions. There is no teaching or working example of a particular disease state in which the compositions can be administered to achieve a particular effect, nor is there any teaching of the amount of the particular composition to be administered, the modes of administration, or the expected outcome of such a treatment. Moreover, as the function of v-IL-6 is not known, one of skill in the art would not know, *a priori*, what effect administration of v-IL-6 or a nucleic acid sequence encoding v-IL-6 would have on a subject. In addition, administration of a pharmaceutical composition comprising a nucleic acid sequence encoding v-IL-6 encompasses gene therapy. The state of the art at the time of filing clearly indicates that the art of gene therapy is neither routine nor predictable. In the "Report and Recommendations of the Panel to Assess the NIH Investment in Research on Gene

Therapy" (published December 7, 1995), Orkin and Motulsky indicate that clinical efficacy has not been definitively demonstrated at this time in any gene therapy protocol; that major difficulties of gene therapy include shortcomings in all current gene transfer vectors and an inadequate understanding of the biological interaction of these vectors with the host; that it is not always possible to extrapolate directly from animal experiments to human studies; and that while the most straight-forward application of gene therapy may be in the treatment of single-gene inherited disorders, practical difficulties need to be addressed, i.e. delivery of the appropriate gene to a specific cell type or tissue, gaining access to the relevant cell type for correction of the defect, assessing the total fraction of cells in a tissue that need to be corrected, achieving the level of expression required for correction, and regulating expression of the added gene once it is transferred into appropriate target cells (see, e.g., pages 1 and 2, points 2, 3, and 5, for example, page 5, under "Single-gene inherited disorders", and page 14, bullet paragraphs 3-6). Similarly, Verma *et al.* (Nature, 387:239-242, 1997) indicate that "In principle, gene therapy is simple: putting corrective genetic material into cells alleviates the symptoms of disease. In practice, considerable obstacles have emerged; problems such as lack of efficient delivery systems, lack of sustained expression, and host immune response reactions remain formidable challenges; although more than 200 clinical trials are currently underway worldwide, with hundreds of patients enrolled, there is no single outcome that we can point to as a success story" (see page 239, under Abstract, and left column, paragraphs 1-2). In view of the of the unpredictability of the effectiveness of gene therapy, and the lack of guidance in the specification of how to make and use the therapeutic agents for gene therapy, one of ordinary skill in the art would not know how to use the claimed pharmaceutical compositions.

Claims 20, 34, and 35 are directed to cell culture media comprising v-IL-6 and methods of culturing cells in medium comprising a cell-growth-stimulating amount of v-IL-6. The claims are not enabled for the media or methods of culturing cells as the

specification does not disclose the functional activity of v-IL-6 or what a cell growth-stimulating amount of v-IL-6 encompasses. As providing suitable cell culture media and suitable cell culture conditions for stimulating the growth of cells is dependent on cell type and must be determined empirically (see for example, sections 3.2.4, and section 4 of Maurer, in Animal Cell Culture, A Practical Approach, ed. R.I. Freshney, IRL Press Limited, 1986) one of skill in the art would not know how to use the cell culture medium or practice the method of culturing the cells without undue experimentation.

Claim 28 is directed to a fragment of a polypeptide obtainable by recombinant expression of the DNA of HHV-8 and which comprises the amino acid sequence of Figure 2. The claim is not enabled as the specification does not disclose polypeptides obtainable by recombinant expression of the DNA of HHV-8 which comprises but is not limited to the viral-IL-6 polypeptide, thus, the specification does not disclose how to make the fragment nor does the specification disclose how to use the fragment. Given the lack of guidance in the specification, it would require undue experimentation for the skilled artisan to make and use a fragment without knowledge of the function of the fragment.

Given the limited guidance in the specification, and the state of the art of the biological function of HHV8 viral-IL-6 and the cellular homologue, IL-6, one of skill in the art could not make or use the viral-IL-6 peptide or fragments thereof, or the compositions comprising nucleic acid sequences encoding v-IL-6 without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12, 16, 18-20, 28, 34, and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2 , 9, 10, and 28 are rendered vague and indefinite by the phrase "which can be obtained by (or which is obtainable by) recombinant expression of the DNA of human herpes virus type 8 (HHV-8)" as it is unclear if the entire genome is used for recombinant expression or if a plasmid comprising a polynucleotide comprising the ORF encoding viral IL-6 is used for expression.

Claims 2, 3, 10, and 28 are rendered vague and indefinite as there is no amino acid sequences set forth in Figure 2. It is unclear which amino acid sequences applicants are claiming.

Claim 4 is rendered vague and indefinite by the phrase "having the capability of binding" as it is unclear under what conditions the fragment is capable of binding to an IL-6 receptor. It is also unclear which fragment of v-IL-6 binds to the IL-6 receptor.

Claims 4 and 5 are rendered vague and indefinite by the use of upper case and lower case letters designating the amino acids. It is unclear what the distinction is between the uppercase and lower case amino acid designations. Clarification is required.

Claim 7 is rendered vague and indefinite by the phrase "mutants and variants of v-IL-6 as claimed in claim 1"" as there are no mutants or variants recited in claim 1. The phrase lacks antecedent basis. The claim is also rendered vague and indefinite by the phrase "conventional amino acid substitutions or deletions" as it is unclear what are the conventions upon which applicants are relying. Moreover, it is unclear what is intended by "functionally equivalent" as there is no teaching in the specification as to what the specific functions of v-IL-6 encompass. The metes and bounds of the claims are unclear as it is unclear to what extent v-IL-6 could be altered such that mutants and variants of v-IL-6 are functionally equivalent.

Claim 8 is rendered vague and indefinite for the following reasons: the phrase "a fragment of the v-IL-6 as claimed in claim 1" is vague and indefinite as it lacks antecedent basis, i.e., there are no fragments recited in claim 1; the phrase "characterized in that" is vague and indefinite

because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d); the term "competively" renders the claim vague and indefinite as this does not appear to be an art-recognized term, thus it is unclear what type of inhibition is intended. To expedite prosecution, the examiner will assume that "competively" is a typographical error and that applicants intended the term "competitively". The phrase "competively inhibit the biological activity of IL-6" renders the claim vague and indefinite as it is unclear if one fragment of v-IL-6 can inhibit all biological activities of IL-6 or if there is a correlation between the amino acid sequence of the fragment and the ability of that particular sequence to inhibit a particular biological activity. It is also unclear what type of assay is suitable for the competitive inhibition of the biological activity of IL-6.

Claim 11 is rendered vague and indefinite by the phrase "the nucleotide sequence of Figure 2" as there is no nucleotide sequence depicted in Figure 2. It is unclear what nucleotide sequence applicants are claiming.

Claim 12 is rendered vague and indefinite for the following reasons: it is unclear what conditions applicants intend as "stringent" as there is no definition either in the claim or in the specification as to which hybridization conditions are deemed "stringent conditions"; it is unclear if the phrase "encoding functional v-IL-6" is describing the nucleic acid of claim 11 or the isolated nucleic acid molecule which hybridizes to the nucleic acid of claim 11.

Claim 16 is rendered vague and indefinite because only one component of the testkit is recited, i.e., the nucleic acid molecule of claim 11. As the testkit is to detect v-IL-6 DNA or RNA, it is unclear how the nucleic acid molecule, in an of itself, can detect v-IL-6 DNA or RNA. There appears to be missing components in the testkit.

Claim 18 is rendered vague and indefinite by the phrase "the polypeptide as claimed in claim 2" as it is unclear which polypeptide is being claimed (see the rejection of claim 2, above).

Claim 34 is rendered vague and indefinite by the phrase "a cell growth-stimulating amount of v-IL-6"" as neither the claim nor the specification discloses any amount of v-IL-6 which

stimulates cell growth of any cell type. Thus, it is unclear what amounts are encompassed in "a cell growth-stimulating amount".

Claim 35 is rendered vague and indefinite by the term "hemopoetic" as this does not appear to be an art recognized term. To expedite prosecution, the examiner will assume that "hemopoetic" is a typographical error and that applicants intended "hemopoietic".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 9-12, 16 are rejected under 35 U.S.C. 102(a) as being anticipated by Zhong *et al.* (Proc. Natl. Acad. Sci., U.S.A., 93:6641-6646, June, 1996).

Claims 9-12 and 16 are directed to an isolated nucleic acid comprising a nucleic acid sequence which encodes herpesvirus type 8 viral interleukin-6 or a composition comprising an isolated nucleic acid comprising a nucleic acid sequence which encodes herpesvirus type 8 viral interleukin-6.

Zhong *et al.* teach the isolated genomic DNA of herpesvirus type 8, and vectors comprising various fragments of the genomic DNA of herpesvirus type 8 (see, e.g., page 6641, right column, under "Materials and Methods").

As the isolated genomic DNA of herpesvirus type 8 comprises an open reading frame encoding viral interleukin-6, the reference of Zhong *et al.* anticipates the claimed invention.

Claims 9-12, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Chang *et al.* (Science, 266:1865-1869, 1994) in light of Chang *et al.* (U.S. Patent No. 5,831,064, 1998).

Claims 9-12 and 16 are directed to an isolated nucleic acid comprising a nucleic acid sequence which encodes herpesvirus type 8 viral interleukin-6 or a composition comprising an isolated nucleic acid comprising a nucleic acid sequence which encodes herpesvirus type 8 viral interleukin-6.

Chang *et al.* teach isolated DNA specimens extracted from Kaposi's sarcoma lesions (see, e.g., Science, page 1869, #8 under "References and Notes"). As the DNA specimens necessarily comprise herpesvirus type 8 DNA (see, e.g., Chang *et al.*, U.S. Patent No. 5,831,064, col. 1, line 60 through col. 2, line 23) which inherently comprises an open reading frame encoding viral interleukin-6, and which would necessarily hybridize to an isolated nucleic acid sequence encoding functional v-IL-6, the reference of Chang *et al.* anticipates the claimed invention.

Claim 8 is rejected under 35 U.S.C. 102(b) as being anticipated by Clark *et al.* (WO 88/00206, 1988).

The claim is directed to mutants and variants of v-IL-6 which are functionally equivalent to v-IL-6. As the claim does not recite the extent of mutations and variations, the claim encompasses IL-6.

Clark *et al.* teaches expression of recombinant IL-6 protein (see, e.g., pages 18-22). The recombinant IL-6 protein is necessarily functionally equivalent to v-IL-6 in view of the disclosure of the instant application that V-IL-6 is functionally equivalent to IL-6 (see page xx of the specification).

Thus, the reference of Clark *et al.* anticipates the claimed invention.

Claims 9-12, 16 are rejected under 35 U.S.C. 102(e) as being anticipated by Ganem *et al.* (U.S. Patent No. 5,861,240, 1999, effective filing date of 2/28/96).

Claims 9-12 and 16 are directed to an isolated nucleic acid comprising a nucleic acid sequence which encodes herpesvirus type 8 viral interleukin-6 or a composition comprising an isolated nucleic acid comprising a nucleic acid sequence which encodes herpesvirus type 8 viral interleukin-6.

Ganem *et al.* teach the isolated genomic DNA of herpesvirus type 8 (see, e.g., col. 9, lines 11-13), which inherently contains a nucleic acid sequence encoding viral interleukin-6.

As the isolated genomic DNA of herpesvirus type 8 comprises an open reading frame encoding viral interleukin-6, the reference of Ganem *et al.* anticipates the claimed invention.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant is requested to return a copy of the attached Notice to Comply with the response.

The application also fails to comply with the requirement of 37 CFR 1.821(d) as reference must be made to the sequences disclosed in Figures 1 and 2 in the text of the description of the Figures, or in the Figures themselves, by use of a sequence identifier, preceded by "SEQ ID NO:". Note that the consensus sequence depicted in Figure 1 must also be identified by a sequence identifier preceded by "SEQ ID NO:". Reference must also be made to the sequences of claims 4 and 5 by use of a sequence identifier preceded by "SEQ ID NO:".

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet M. Kerr whose telephone number is (703) 305-4055. Should the examiner be unavailable, inquiries should be directed to John LeGuyader, Supervisory Primary Examiner of Art Unit 1633, at (703) 308-0447. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 305-7401. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633.

Janet M. Kerr, Ph.D.
Patent Examiner
Group 1600

JOHN L. LeGUYADER
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Application No.:09/230,048

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.
- [X] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- [X] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- [ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- [ ] 7. Other: the topology of the sequence was not reported.

Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- [X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

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